

**In The Claims:**

Please amend claim 1, 11, 26, 39, 70 and 71, cancel claims 5 and 6 (without prejudice), and add new claims 82 and 83 as provided below in the associated claim listing on separate sheets:

1. (Currently amended) A method of analyzing tissue, the method comprising:

illuminating a tissue with coherent or partially coherent light;

receiving light reflected from the tissue at a detector and forming series of speckle patterns;

and

analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by microscopic motion of objects within the tissue, wherein the tissue is at least one of in vivo or an internal tissue.

2. (Previously presented) The method of claim 1, wherein the microscopic motion is Brownian motion.

3. (Previously presented) The method of claim 1, wherein the microscopic motion is motion of cells or cellular organelles.

4. (Previously presented) The method of claim 1, further comprising compensating for macroscopic motion to isolate the microscopic motion.

Claims 5 and 6 (Cancelled).

7. (Previously presented) The method of claim 6, wherein the illuminating step comprises providing an invasive device coupled to a light source, passing the device into a patient, placing the device in proximity to the tissue, and shining coherent or partially coherent light from the light source onto the tissue.

8. (Previously presented) The method of claim 7, wherein the invasive device is selected from the group consisting of a catheter, an endoscope, and a laparoscope.

9. (Previously presented) The method of claim 7, wherein the placing step includes placing the device in direct contact with the tissue.

10. (Previously presented) The method of claim 1, wherein the coherent light comprises laser light.

11. (Currently amended) A The method of claim 1 of analyzing tissue, the method comprising:  
illuminating a tissue with coherent or partially coherent light;  
receiving light reflected from the tissue at a detector and forming series of speckle patterns;  
and  
analyzing changes in the speckle patterns at time intervals sufficient to measure changes  
caused by microscopic motion of objects within the tissue, wherein the partially coherent light  
comprises light from a superluminescent diode.

12. (Previously presented) The method of claim 1, wherein a detector is located farther than one wavelength of light from the tissue and detects far field speckle.

13. (Previously presented) The method of claim 1, wherein a detector is located within one wavelength of light from the tissue and detects near field speckle.

14. (Previously presented) The method of claim 1, wherein the analyzing step comprises comparing each of the series of speckle patterns to a series of reference speckle patterns, and quantifying the temporal correlation differences between the speckle patterns and the reference patterns.

15. (Previously presented) The method of claim 14, wherein the analyzing step comprises digitizing each of the speckle patterns, and the quantifying step comprises evaluating a cross-correlation between the speckle patterns and the reference patterns.

16. (Previously presented) The method of claim 14, wherein the analyzing step comprises digitizing each of the speckle patterns, and the quantifying step comprises evaluating a maximum cross-correlation between the speckle patterns and the reference patterns.

17. (Previously presented) The method of claim 15, wherein the analyzing step further comprises determining a decorrelation rate for the speckle patterns.

18. (Previously presented) The method of claim 1, wherein the analyzing step further comprises analyzing spatial characteristics of the speckle pattern to deduce structural characteristics of the tissue.

19. (Previously presented) The method of claim 1, wherein the analyzing step further comprises analyzing spatial characteristics of the speckle pattern to deduce biomechanical characteristics of the tissue.

20. (Previously presented) The method of claim 18, wherein the illuminating step comprises illuminating multiple locations of the tissue in succession, the receiving step comprises forming a separate series of speckle patterns for each respective section of the tissue, and the analyzing step comprises analyzing each separate series of speckle patterns and comparing the separate series to deduce structural differences between the respective locations of the tissue.

21. (Previously presented) The method of claim 4, wherein compensating for macroscopic motion comprises performing the receiving step during a diastole of a heartbeat.

22. (Previously presented) The method of claim 4, wherein macroscopic motion comprises patient motion.

23. (Previously presented) The method of claim 4, wherein the macroscopic motion is peristalsis.

24. (Previously presented) The method of claim 4, wherein receiving comprises gathering reflected light at a light receptor and transmitting the gathered light to a detector, and wherein compensating for macroscopic motion includes coupling the receptor to the tissue.

25. (Previously presented) The method of claim 4, wherein compensating for macroscopic motion includes excluding changes in the speckle patterns caused by non-random motion during the analysis step.

26. (Currently amended) ~~A~~ The method of claim 4 of analyzing tissue, the method comprising:

illuminating a tissue with coherent or partially coherent light;

receiving light reflected from the tissue at a detector and forming series of speckle patterns;

analyzing changes in the speckle patterns at time intervals sufficient to measure changes

caused by microscopic motion of objects within the tissue; and

compensating for a macroscopic motion to isolate the microscopic motion, wherein the  
macroscopic motion results from a motion or the deformation of blood flow between the tissue and  
the reflector, and the compensating step comprises replacing the blood with a transparent solution.

27. (Previously presented) The method of claim 1, wherein the tissue comprises an atherosclerotic plaque.

Claims 28 –38 (Cancelled).

39. (Currently amended) A method of analyzing a tissue structure, the method comprising:

illuminating the tissue structure with coherent or partially coherent light;  
receiving light reflected from the tissue structure at a detector and forming a series of speckle patterns;  
gathering speckle pattern data at time intervals sufficient to measure microscopic motion within the tissue structure or adjacent tissue; and  
assessing the tissue structure by analyzing spatial characteristics of the speckle pattern data to deduce structural or biomechanical characteristics of the tissue structure, wherein the tissue structure is at least one of in vivo or an internal tissue structure.

40. (Previously presented) The method of claim 39, wherein analyzing comprises assessing the thickness of the tissue structure.

41. (Previously presented) The method of claim 40, wherein tissue structure thickness is assessed by

- (i) measuring the decorrelation time constant  $r$  as a function of  $r = (x_o^2 + y_o^2)^{1/2}$ ;
- (ii) measuring optical properties of the tissue structure; and
- (iii) comparing the measured optical properties and  $\tau(r)$  to a mathematical simulation that models light remittance as a function of tissue structure thickness.

42. (Previously presented) The method of claim 41, wherein the optical properties are measured by computing first and second order statistics of a speckle probability distribution function or by using diffuse reflectance spectrophotometry.

43. (Previously presented) The method of claim 41, wherein the mathematical simulation is a Monte Carlo simulation or diffusion theory simulation.

Claims 44-61 (Cancelled).

62. (Previously presented) The method of claim 27, further comprising gathering speckle pattern data at time intervals sufficient to measure microscopic motion within a lipid pool within the atherosclerotic plaque; and assessing the atherosclerotic plaque's vulnerability to rupture from the amount of microscopic motion.

63. (Previously presented) The method of claim 62, further comprising analyzing spatial characteristics of the speckle pattern data to deduce structural characteristics of the plaque.

64. (Previously presented) The method of claim 63, wherein analyzing comprises assessing the thickness of the fibrous cap.

65. (Previously presented) The method of claim 64, wherein cap thickness is assessed by

- (i) measuring the decorrelation time constant  $\tau$  as a function of  $r = (x_o^2 + y_o^2)^{1/2}$ ;
- (ii) measuring optical properties of the cap; and
- (iii) comparing the measured optical properties and  $\tau(r)$  to a mathematical simulation that models light remittance as a function of cap layer thickness.

66. (Previously presented) The method of claim 65, wherein the optical properties are measured by computing first and second order statistics of a speckle probability distribution function or by using diffuse reflectance spectrophotometry.

67. (Previously presented) The method of claim 65, wherein the mathematical simulation is a Monte Carlo simulation or diffusion theory simulation.

68. (Previously presented) The method of claim 64, wherein a plaque is considered vulnerable to rupture if the thickness of the fibrous cap is less than about 60 microns.

69. (Previously presented) The method of claim 63, wherein analyzing comprises assessing the viscosity of the lipid pool.

70. (Currently amended) A The method of claim 69, of analyzing tissue, the method comprising:  
illuminating a tissue with coherent or partially coherent light, wherein the tissue comprises an  
atherosclerotic plaque;  
receiving light reflected from the tissue at a detector and forming series of speckle patterns;  
and  
analyzing changes in the speckle patterns at time intervals sufficient to measure changes  
caused by microscopic motion within a lipid pool within the atherosclerotic plaque; and assessing  
the atherosclerotic plaque's vulnerability to rupture from the amount of microscopic motion, wherein  
the plaque is considered vulnerable to rupture if the viscosity of the lipid pool has a time constant of less than about 200 milliseconds.

71. (Currently amended) A The method of claim 69, of analyzing tissue, the method comprising:

illuminating a tissue with coherent or partially coherent light, wherein the tissue comprises an atherosclerotic plaque;

receiving light reflected from the tissue at a detector and forming series of speckle patterns;  
and

analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by microscopic motion within a lipid pool within the atherosclerotic plaque; and assessing the atherosclerotic plaque's vulnerability to rupture from the amount of microscopic motion, wherein the plaque is considered likely to rupture if the viscosity of the lipid pool has a time constant of less than about 100 milliseconds.

72. (Previously presented) The method of claim 39, wherein the tissue structure comprises an atherosclerotic plaque.

73. (Previously presented) The method of claim 40, wherein tissue structure thickness is assessed by analyzing variation of  $\tau$  as a function of distance from a center of the speckle pattern as a function of  $(x_0^2 + y_0^2)^{1/2}$ .

74. (Previously presented) The method of claim 64, wherein thickness of the fibrous cap is assessed by analyzing variation of  $\tau$  as a function of distance from a center of the speckle pattern as a function of  $(x_0^2 + y_0^2)^{1/2}$ .

75. (Previously presented) The method of claim 1, wherein analyzing comprises measuring biomechanical properties of the tissue in three dimensions.

76. (Previously presented) The method of claim 39, wherein analyzing comprises measuring biomechanical properties of the tissue in three dimensions.

77. (Previously presented) The method of claim 1, wherein analyzing comprises determining collagen content of the tissue.

78. (Previously presented) The method of claim 1, wherein analyzing comprises determining viscosity of a lipid pool within the tissue.

79. (Previously presented) The method of claim 39, wherein analyzing comprises determining collagen content of the tissue.

80. (Previously presented) The method of claim 39, wherein analyzing comprises determining viscosity of a lipid pool within the tissue.

81. (Previously presented) The method of claim 62, wherein the microscopic motion is Brownian motion or cellular motion.

82. (New) A of analyzing tissue, the method comprising:

illuminating a tissue with coherent or partially coherent light;

receiving light reflected from the tissue at a detector and forming series of speckle patterns;  
analyzing changes in the speckle patterns at time intervals sufficient to measure changes  
caused by microscopic motion of objects within the tissue; and  
at least partially replacing blood provided in or adjacent to the tissue with at least partially  
transparent solution.

83. (New) A of analyzing tissue, the method comprising:

illuminating a tissue with coherent or partially coherent light;  
receiving light reflected from the tissue at a detector and forming series of speckle patterns;  
analyzing changes in the speckle patterns at time intervals sufficient to measure changes  
caused by microscopic motion of objects within the tissue;  
compensating for a macroscopic motion to isolate the microscopic motion, wherein the  
macroscopic motion results from a motion or the deformation of the tissue; and  
at least partially replacing blood provided in or adjacent to the tissue with at least partially  
transparent solution.